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| 10/539,443 | 06/20/2005 | Anders Nykiaer | NYKJAER1 | 6823 |

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| EXAMINER | |
|---|---|
| MACFARLANE, STACEY NEE | |
| ART UNIT | PAPER NUMBER |
| 1649 | |

| MAIL DATE | DELIVERY MODE |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/539,443 | NYKIAER ET AL. | |
| | Examiner | Art Unit | |
| | STACEY MACFARLANE | 1649 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *14 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *73,78,81-86,88-98 and 100* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *73,78,81-86,88-98 and 100* is/are rejected.

7)☒ Claim(s) *81* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/13/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/14/2008 has been entered.

### *Response to Amendment*

2. Claims 73, 78, 81, 83, 84, 88, 90, 91 and 94 have been amended as requested in the amendment filed on October 14, 2008. Following the amendment, claims 73, 78, 81-86, 88-98 and 100 are pending in the instant application.

Claims 73, 78, 81-86, 88-98 and 100, in so far as they read upon the elected species: an antibody agent directed against a sequence of SEQ ID NO: 1, Sortilin, the neurotrophin NGF and wherein the condition is an “injury and/or dysfunction of the central and/or peripheral nervous system”, are under examination in the instant office action.

3. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

4. Applicant's arguments filed on October 14, 2008 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

### *Claim Objections*

5. Claim 92 and 95 are objected to for recitation of non-elected subject matter.

6. Claim 81 is objected to because of the following informalities: Line 3 of the claim has a period in the middle. See MPEP section 608.01(m), "Each claim begins with a capital letter and ends with a period. Periods may not be used elsewhere in the claims except for abbreviations. See *Fressola v. Manbeck*, 36 USPQ2d 1211 (D.D.C. 1995)". Appropriate correction is required.

### *Claim Rejections - 35 USC § 112*

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claim 81 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim is vague and indefinite in that it recites "nerve damage aberrant sprouting in epilepsy". This condition is not know in the art and the metes and bounds are indecipherable.

### *Claim Rejections - 35 USC § 112*

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. As currently amended, Claims 73, 78, 81-86, 88-98 and 100 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an in vitro method comprising exposing a receptor of the Vps10p-domain family to an antibody thereby inhibiting the binding of a proneurotrophin to the receptor, does not reasonably provide enablement for the method in vivo nor in any animal suffering from an injury or dysfunction of the central or peripheral nervous system, as required by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

On pages 5-9 of Remarks filed October 14, 2008, Applicant traverses the rejection on the grounds that "Applicant need only show a reasonable expectation of success for antibody binding to the receptor" in order to be enabled for the method as claimed and "methods of making and screening antibodies are preformed routinely by those of skill in the art and accordingly do not need to be specifically disclosed in the instant application". Applicant further argues that methods comprising administration of antibodies in vivo and their ability to cross the blood-brain barrier were well-known in the art prior to filing. While these arguments have been fully considered they are not found persuasive to overcome the rejection for the following reasons.

In *Hoffer v. Microsoft Corp.*, 405 F.3d 1326, 1329, 74 USPQ2d 1481, 1483 (Fed. Cir. 2005), the court held that when a whereby or wherein clause "states a condition that is material to patentability, it cannot be ignored in order to change the substance of the

invention." While, in general, claim scope is not limited by claim language that suggests or makes optional particular steps, language that structurally or materially limits the claim is given weight. Such is the case here where the method of the claims is materially limited to exposing a receptor in a specific subset of animals, "animal suffer[ing] from an injury or dysfunction of the central or peripheral nervous system", to an antibody that binds said receptor. Therefore, the nature of the invention is drawn to treatment of an injury or dysfunction of the central or peripheral nervous system comprising in vivo exposure to an antibody raised against a receptor of the Vps10p-domain family. Dependent claims specifically recite the animal of the claims can suffer from a long list of encompassed pathological conditions, such as, Alzheimer's disease, Parkinson's disease, Huntington's chorea, stroke, ALS, paralysis, peripheral neuropathies, necrosis or loss of neurons, nerve damage aberrant sprouting in epilepsy, schizophrenia, epilepsy, multiple sclerosis, Down's Syndrome, nerve deafness, Meniere's disease, or neuropathies attributed to gastrointestinal tract, atony of the urinary bladder, post-polio syndrome, and AIDS, or hereditary neuropathies such as Charcot-Marie- Tooth disease, Refsum's disease, Abetalipoproteinemia, Tangier disease, Krabbe's disease, Metachromatic leukodystrophy, and Dejerine-Sottas syndrome. Thus, the claims broadly encompass methods for the treatment of any injury or dysfunction of the central or peripheral nervous system comprising administering any antibody to a Vsp10p-domain receptor and inhibiting the binding of any neurotrophin. As such the scope of the methods is that it can be successfully performed in an unreasonable number of pathologically distinct conditions, both acute conditions

presumably requiring acute modes of antibody administration and hereditary conditions that would presumably require chronic exposure to said antibody.

The invention is based on the finding that modulation of the Vps10p-domain receptor family affects neurotrophin or pro-neurothrophin activity. The instant specification provides no evidence of a single specific antibody that binds to a receptor of the Vps10p-domain receptor family, nor does it provide evidence that such binding mediates a physiological effect that could be used in any animal suffering from an injury or dysfunction. For many of the broadly encompasses dysfunctions or injuries there is no evidence within the art of a nexus between Vsp10p-domain receptor function and disease etiology, pathology or symptomology. Thus, there is no evidence of record that exposing a receptor of the Vps10p-domain receptor family to an antibody that binds said receptor and subsequently inhibits the binding of a proneurotrophin, would mediate any in vivo effect, as claimed. Furthermore, the specification provides no guidance or working examples of any specific antibody, nor does the disclosure provide guidance or direction that the method was successfully achieved in vivo or present evidence of an in vitro model that would be predictive of success in vivo. Absent such guidance, one of ordinary skill in the art would require undue experimentation to discover how to practice Applicant's invention, as currently claimed.

The state of the art at the time of filing was unclear as to the physiological role of the Vps10p-domain receptor family. On page 4 of the instant specification, Applicant states “some progress has been made as to an understanding of the role of this family [of receptors]”. Examiner maintains, for reasons of record in the Paper mailed

10/24/2007, that, at the time of filing, the state of the art with respect to a function of these Vsp10-domain receptors was speculative at best. Prior to filing, it was known that Vps10p-domain receptors are capable of binding antibodies in vitro (Jacobsen et al., The Journal of Biological Chemistry, 271(49):31379-31383, December 6, 1996; Nielsen et al., The Journal of Biological Chemistry, 274(13):8832-8836, March 26, 1999).

While the skill level in the art is high, the level of predictability is low. Examiner does not refute the clinical use of monoclonal antibodies and even specific modifications that may deliver antibodies across the blood-brain barrier as stated in Remarks pages 8-9, however, in order for an antibody to cross the blood-brain barrier it requires both specificity and modification or engineering. The instant specification fails to identify even one antibody that can be used in the method, and broadly claims that any antibody that binds to the Vps10p-domain family of receptors can be used with a reasonable expectation of success. Since even the current art teaches that unpredictability remains and that specificity and validation are crucial for a reasonable expectation of success for the use of antibodies as CNS therapies, then one of ordinary skill in the art would have to rely on the guidance within the instant specification in order to practice the method as claimed. However, the instant disclosure has not provided guidance as to how the invention may be practiced to the full scope of the claims.

The standard of an enabling disclosure is not the ability to make and test if the invention works but one of the ability to make and use with a reasonable expectation of success. A patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. In the

decision of *Genentech, Inc, v. Novo Nordisk*, 42 USPQ 2d 1001, (CAFC 1997), the court held that:

> "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure". The court further stated that "when there is no disclosure of any specific starting material or of any of the conditions under which a process is to be carried out, undue experimentation is required; there is a failure to meet the enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art", "[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".

Examiner concludes that the instant specification is not enabling because one cannot follow the guidance presented therein and practice the claimed method without first making a substantial inventive contribution. In the instant case, one of ordinary skill in the art would have to first correlate Vps10p receptor blockade with the pathology of an injury or dysfunction of the central or peripheral nervous system, develop an antibody that binds said receptor and inhibits the binding of a pro-neurotrophin to said receptor, successfully expose CNS and PNS receptors to said antibody, and demonstrate a useful effect in an animal suffering from an injury or dysfunction in order to practice the method as claimed. Such experimentation is not routine but constitutes

undue experimentation in order to close the gaps between genetic, laboratory, and clinical data.

***Conclusion***

11. No Claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to STACEY MACFARLANE whose telephone number is (571)270-3057. The examiner can normally be reached on M-W and ALT F 5:30 to 3:30, TELEWORK-Thursdays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Stacey MacFarlane
Examiner

Art Unit 1649

/John D. Ulm/
Primary Examiner, Art Unit 1649